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WOUND INFECTION: THE CAUSES WHICH PREDISPOSE TO ITS PRODUCTION, OR FAVOR IMMUNITY, AND THE ROLE OF ANTISEPTIC AGENTS.[1]

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THE study of wound infection is inseparable from that of immunity from the same, and when we have learned that which constitutes or favors immunity, we shall approach nearer that which is now a *terra incognita.* As Brunton has well said, in his recent address before the British Medical Association, "immunity is a complex condition not dependent upon any single factor," and from pathological interest, as well as from clinical importance, our endeavor now must be to analyze the main question, of what constitutes or confers immunity, and try to first recognize and then solve its various subordinate queries.

This statement, too, is inseparable from another, which is to the effect that the surgery of to-day should aim to be *aseptic,* strictly speaking, and not merely *antiseptic;* in other words, we should abolish sepsis, and not merely aim to antidote it or conquer it when present.

The only excuse for surgery which is not strictly aseptic should be met with in cases of injuries where sepsis in some form has already occurred, or those where continuous aseptic precautions are impossible; as, for example, in the mouth, rectum, etc., or in military practice, where the exigencies of the occasion do not permit that which we would ordinarily carry out with precision.

The condition of sepsis itself is a most complicated one, consisting, as far as we now see, of a condition of poisoning by ptomaines, toxines, and albumoses having widely varying strength and properties, some of which are so antagonistic in physiological action to others, that one may neutralize another, as it is well known often occurs. Some of these substances are perfectly harmless in their proper places, but deadly in others. The chemical processes going on within our bodies are as complex and as difficult of appreciation as are those mental processes which so bewilder us when sometimes we endeavor to study and read the character of various individuals. Virchow, in his address before the Tenth International Congress, voiced the general sentiment when he said: "The scientific problems of medicine are, for the most part, centred about the determination of the biological peculiarities of animal and vegetable cells." (*Vide* paper by Braatz, *Deutsche med. Wochenschrift*, 1891, No. 22.) "Lépine has lately shown that while the pancreas is pouring into the digestive channel the ferment which will form sugar, it is at the same time emptying into the system another ferment which will destroy it." (Brunton.)

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[1] An address delivered before the Second Triennial Congress of American Physicians and Surgeons, at Washington, D. C., September 22, 1891.

But this is no more than is constantly happening in the alimentary canal, into which the intestinal glands are constantly pouring fluids which shall assist in the digestion of ingesta, while the intestinal absorbents may be taking up poisons produced by their mutual reactions. I esteem the proper realization of this fact as of great importance to the surgeon, as well as a due recognition of the organ through which these various poisonous substances are filtered out before reaching the systemic circulation. The physiologists have shown us that the organ by which this is accomplished is the liver, by virtue of its so-called depurative action. This is but one of its multiple functions. I have upon another occasion endeavored to show that it is by virtue of this hepatic function that many cases of septic intoxication in surgical patients are avoided, and that when this function is interfered with, the most promising surgical case may go wrong or even terminate fatally.[1] I have also there endeavored to show that in the division of the general subject of blood-poisoning a condition which we will call, if you please, intestinal toxæmia, or entero-sepsis, deserves a distinct place; that it occurs not infrequently; that by a continuation of it the condition may be merged into one of sapræmia, septicæmia, or pyæmia, and that when promptly antidoted or checked there is a speedy return to a desirable condition, both of wound and of the patient.

All of which leads to a statement upon which I desire to lay all the stress it may bear, which is to this effect—that when we have apparently commencing sepsis we are altogether too prone to look first to the wound itself for an explanation of its origin. I claim—basing this claim upon observation and laboratory study—that by no means all cases of surgical sepsis have their origin in or about the wound, no matter how soon the wound may begin to show changes. To this statement I shall recur after a little.

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[1] "Mütter Lectures on Surgical Pathology." Annals of Surgery, vol. xiii., June, 1891, p. 446.

As bearing on what has already been said, however, I wish to appeal to the personal experience of all those who have done general or special surgery. The very facts that careful surgeons prepare their patients for operation and that those who institute the most careful measures in this direction enjoy the greatest success, are, of themselves, proofs of the strength of this position. And the practice which has obtained from time immemorial in such septic conditions as puerperal fever, and many others, of giving a purgative, by which the alimentary canal is freed of toxic materials and the action of the liver stimulated, is additional evidence in the same direction. However others may interpret these conditions, the individuality of a condition of entero-sepsis is for me too apparent to be contested.

We have learned a little, and have yet much to learn, with reference to the antagonisms of different bacteria and the poisons which they produce. If a microbe can enter the system and produce a proteid or albuminoid poisonous to the animal harboring it, it may there thrive and produce such poison, while the injection or the introduction of some other substance may neutralize this poison and save the animal. The principle involved herein is the same whether the antidotal poison be injected as such, or whether a second species be inoculated by which it may be produced. The study of proteid materials is even yet so occult that we know but little about them. Were the truth concerning all the details of our body chemistry known, we should see in every human being a laboratory in which are going on more processes of manufacture and destruction than can be witnessed even in a World's Fair.

Brunton has suggested that blisters do good in this way, not merely by affecting the circulation, but by an endermic administration of proteids derived, of course, from the blood, but so altered in passage from the vessels as to have a different effect, and probably also, as will be seen, by their chemotactic properties. He also suggests that bleeding may be of benefit in a similar way, since experiments have shown that by abstraction of venous blood there is caused absorption of proteid matters from the tissues, and that these proteids may have an action of their own on tissues with which they may come in contact. The indisputable benefits, in many cases, of free purgation probably finds here also its proper explanation.

I have already introduced a term implying a condition but recently recognized, to which it seems necessary to ask your attention for a few moments. It is known under the name, given it by Pfeffer, of *chemotaxis*, and refers to that faculty possessed by all motile bacteria of moving toward or away from certain substances which seem to attract or repel them. This faculty is, however, by no means confined to the bacteria, since Stahl has shown that the same power is inherent in the plasmodia of myxo-mycetes, as well as in various other unicellular organisms; and what especially concerns us here is the fact that the leucocytes at least, if not various other cells of our own bodies, possess the same property. As yet a general recognition of this fact hardly obtains among the profession, although an elaborate article on the subject has been published recently by Prudden;[1] but it seems to me a matter of common importance to all who study inflammation and its results. Observers in this direction have shown that bacteria, for instance, move toward nutritive material, and this power has been utilized by Ali Cohen to separate motile from immotile bacteria. He filled capillary tubes with positive chemotactic material, like potato-juice, and with this could attract typhoid and cholera bacteria from fæces, and thus make their pure cultivation much easier.

The chemotactic properties of leucocytes remind one very much of the so-called tactile sensibilities which the amœbæ possess, only they enjoy them in perhaps higher degree. Lactic acid, 10 per cent. salt solution, quinine 0.5 per cent., 10 per cent. alcohol, chloroform, glycerin, and bile produce in leucocytes chemotactic activity by which they are repelled. It must be said here that chemotaxis is spoken of as positive or negative, according as there appears to be attraction or repulsion. Among the most actively positive chemotactic substances are cultures of bacteria. These are powerfully attracted by the leucocytes. Hence it appears that bacteria and leucocytes are mutually attractive, and the effect is the same whether the cultures are alive or have been killed by boiling; but it is not the culture medium itself by which this activity is manifested, but by some product of the life and growth of the bacteria.

It has been Buchner's happy lot to widely extend our knowledge of the function and importance of the leucocyte in its chemotactic relations. He has demonstrated that its phagocytic action is but a part of that general power which it possesses of responding to chemotactic attraction and incorporating into itself whatever there is of foreign, dead, or offending material, and then removing it. It matters not that it often perishes in this attempt, that is, it matters not in a logical sense, although a quantity of leucocytes which have thus perished constitute a mass of pus, their dead bodies remaining in this form to show the violence of the conflict, and, as it were, their heroism in the engagement. In other words, it follows from Buchner's researches that the process of resolution is in large measure, or for so much as concerns the solid material resorbed, a matter of chemotactic attraction and its results. Furthermore, that of all substances, that which seems to offer the most attraction for leucocytes is the albuminoid material furnished by bacterial cells

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[1] New York Med. Journ., June 6, 1891, p. 637.

It is this that attracts leucocytes, which are brought to the infected area by a magnetism, so to speak, which they cannot resist. This statement is especially true of proteid or albuminoid materials without reference to alkaloids, etc., produced as special products of individual forms. This is the explanation of those cases of that anomalous and clinically unimportant condition known as non-bacterial suppuration, sometimes produced in the laboratory. It is evidenced in such results as those of Wyssokowitsch, who filtered the fluid off from anthrax cultures and found that the filtrate was not pyogenic, while the solid material was.

By ingenious use of Councilman's tubes Buchner proved for the pneumo-bacillus of Friedländer that its free albuminoid material has a marked pyogenic action, and so with numerous others, especially the staphylococci, the bacillus pyocyaneus, and the typhoid bacillus.

It appears thus that the chemotactic activity of bacteria may be exerted by them whether living or dead. In either case they seem to attract toward them leucocytes which then and thus act as scavengers for the surrounding tissues. Buchner has further shown how vegetable caseins and alkali-albumins possess the same chemotactic possibilities.

I would not detain you with a rehearsal of these facts, interesting and important as they are, were it not that they appear to have a most important bearing upon questions which vitally concern the surgeon. First of all, I do not see how in the light of such researches the possibility of phagocytosis can be denied, and the importance of this process looms up in a flood of light when one discusses the phenomena of suppuration, or of other kinds of infection as well as of recovery or immunity therefrom. In suppuration and in absorption, it is proteid material which attracts the leucocytes, the same being furnished either by bacteria or by disintegrating tissue suffering from other infection. Metschnikoff, assuming the truth of his own theory of phagocytosis, invokes that of chemotaxis to explain immunity and freedom after one attack of a contagious disease. He claims that the variety of chemotaxis is variable, and that positive may be converted into negative, or *vice versa*, and that cells may be attracted to substances in mild form, which in strong form they repel, so that by inoculating with attenuated virus chemotaxis at first negative will change slowly to positive, and the phagocyte will at last be induced to attract and attack the invading element of disease. Whatever may be the final outcome of this perhaps fanciful development of his original theory, it is at least the result of laborious research and patient watching.

Those interested in the phagocyte explanation of conferred immunity will find choice reading in the *Transactions* of the recent International Congress of Hygiene and Demography, where, for instance, Roux, Buchner, Kitasato, and Metschnikoff himself, expounded the views which have set students the world over to thinking and to renewed investigation, and which have made their originators famous. Let it be enough for our present purpose to say that the theory of phagocytosis appears to be more strongly grounded than ever, and that were we deprived of the theory, though acquainted with the facts which corroborate it, we should be at great loss for any rational explanation of the same.

Support of the phagocyte theory has also come from another source, namely, from Hankin's recent work on *Defensive Proteids.* From the spleens and livers of various animals he has isolated the proteid which has the power of killing bacteria, and he has found that this, though absent from normal blood, could be obtained from that of febrile animals. There follow from these facts, if true, various deductions as to the impolitic course of too strenuous efforts to reduce fever in septic cases, upon which, if there were time, one might wish to dwell. This also agrees with Hankin's suggestion that phagocytes not only kill microbes which they have taken in, but can also, by liberating their contents, exert a bactericidal action. It also makes plausible the view that animals that are refractory to particular diseases have the power of producing some particular variety of defensive proteid. There is here opened a most attractive though difficult field for study.

The next important bearing of these views is with reference to the absorption and separation of dead or dying materials, such as large sloughs after extensive burns. These, of course, are loosened by physiological processes in which the formation of proteid material figures largely. By the positive chemotactic properties already alluded to, this attracts leucocytes in large quantities and brings them in numbers where they are needed for tissue repair, and at the same time explains, perhaps, the poisoning with which in these cases we have to deal.

A third not less important bearing is on the use of so-called antiseptic agents. The ideal antiseptic is probably blood serum; its parasiticide properties being, in all probability, connected with the existence in it of a globulin which is only soluble in a weak solution of common salt. This, by the way, may explain the well-known antiseptic action of common salt, and, as Spencer Wells has said, may strengthen the belief that we have in dilute saline solutions a safe and useful fluid for surgical irrigation, preferable to water which has been sterilized simply by boiling, and to various other solutions which may irritate the tissues.

I am not aware that as yet any systematic study of the various antiseptic materials now in general use by surgeons, with reference to their chemotactic activities, has been made. It strikes me, however, that such a study offers the greatest promise of aid in the decision as to what antiseptic to use. But it will be easily seen that once having appreciated this peculiar attraction or repulsion between organized or unorganized materials, we shall have reason to hesitate and reflect before we apply to fresh, raw surfaces, which are supposed to be free from infection, materials, *i. e.*, antiseptic agents, of a character which may disturb the ordinary physiological course of events by begetting such inordinate excitement, serous outpour, and gathering of the leucocytes, as we have seen may occur.

Although it be here a digression, I cannot avoid for a moment stopping to epitomize some of Hankin's recent work, as well as that of Behring and Kitasato, concerning blood serum and its properties.

The work of Buchner and Nissen showed that the bactericidal action of pure blood serum is an important factor in the conflict between the microbe and the animal organism. This has been further confirmed by Bouchard, who showed that the serum of a rabbit will serve as a culture medium for the bacillus pyocyaneus; but if a rabbit be made immune against the diseases caused by this bacillus, the bacillus can no longer be cultivated on the serum of that particular animal. In other words, by making an animal immune against a disease the bactericidal action of its serum is greatly increased. This is true also in the case of cholera, anthrax, hog-cholera, and other diseases. The investigations of Behring and Kitasato have yielded astonishing results. They found that the serum of a rabbit which had been made immune to diphtheria or to tetanus exerts no bactericidal action on the bacilli of these diseases; but that it does possess the remarkable power of destroying the poisons produced by these microbes. In other words, that such serum has *antitoxic* and *not bactericidal* power, and by taking advantage of such power Behring has cured mice of tetanus in which the disease had so far progressed that two or three limbs were in a condition of spasm. Hankin, in a very recent address (*Lancet*, August 15, 1891, p. 339), in discussing this topic, gives the following definition of immunity in the light of recent study: "Immunity, whether natural or acquired, is due to the presence of substances which are formed by the metabolism of the animal rather than by that of the microbe, and which have the power of destroying either the microbe against which immunity is possible, or the products on which their pathogenetic action depends." In giving this definition he expressly states that it is not comprehensive for all instances, and that in some animals immunity against certain diseases depends wholly or in part upon their causes.

He then goes on to briefly describe how he was able to separate from serum the particular compound which conferred this power. He finally narrowed it down to and isolated a particular ferment-like proteid, known as cell-globulin B. And he further showed how this and other defensive proteids in animals, and we may conclude also in man, can be altered in amount by various conditions of diet, environment, etc.

For these defensive proteids Buchner has suggested the name *alexine;* but Hankin would discriminate between them more carefully, and has divided them into those which occur naturally in normal animals, which he proposes to call *sozins*, and those occurring in animals that have been articially made immune—these he would term *phylaxins*. The former he has found in all animals yet examined. He further shows how each of these classes can be subdivided into those that act on bacteria and those that act on the poisons they generate. These sub-classes he would denote by the prefixes *myco-* and *toxo-;* thus *mycosozins* are proteids of the normal animal which have the power of destroying various bacteria, and *toxosozins* are proteids occurring also in the normal animal, which destroy or antagonize the poisons of bacterial origin. Similarly *mycophylaxins* and *toxophylaxins* will denote the classes of the phylaxins.

It has already been stated that by no means all the sources of sepsis concern the wound itself. It is necessary now to classify and briefly allude to the principal reasons why a wound, or a patient who suffers from it, may not be able to resist infection from other sources; or, in other words, to mention the principal other sources of infection possible. These I would classify as follows:

1. Previous long-existent toxæmia (*e. g.*, syphilis, diabetes, acetonæmia, lithæmia, alcoholism, malaria).
2. Previous anatomical changes which reduce vitality (*e. g.*, inherited diatheses, old age, amyloid change, chronic and acute nephritis).
3. Recent or acute toxæmia (uræmia, typhoid, intestinal toxæmia, stercoral toxæmia).
4. Other acute conditions (starvation, scurvy, anæmia).
5. Conditions of environment (bad hygienic surroundings).
6. Effect of anæsthetics.
7. Effect of antiseptics.

1. *Previous long-existent toxæmia.* The disastrous results of operating upon diabetic patients, as well as those presenting active manifestations of syphilis, have long been recognized by surgeons. Nor does one deliberately operate on patients suffering from chronic alcoholism or malaria, if he can avoid it. Other conditions which deserve to be mentioned here as having an occasional yet distinct bearing in this direction are lithæmia, cholæmia, acetonæmia, and the various conditions which are represented by the presence of the oxalates, uric acid, acetone and peptone in the urine.

2. *Previous anatomical changes which lower vitality.* Old age, with its accompanying arterial sclerosis, its cardiac debility, and other well-known tissue alterations, favors sluggishness of wound repair, leads not infrequently to sloughing or to bedsore, and predisposes toward sepsis. Amyloid changes betoken impaired vitality, and chronic or acute nephritis implies that excretion may be interfered with, and some form of toxæmia thereby induced. The inherited diatheses, including tuberculosis and syphilis, may or may not be factors of considerable importance in this respect.

3. *Recent toxæmia.* To illustrate this class of cases a little better, let me mention an illustrative case: A middle-aged woman, of healthy antecedents, recently convalescent from typhoid, which had run an average course, presented a rapidly growing tumor (sarcoma) in one breast. So rapid was its growth that operation could not be delayed. It was made with every aseptic precaution. Nevertheless the skin flaps, which would ordinarily have united without pus, necrosed completely, and left a large surface to heal by granulation.

No one would wittingly operate on a patient suffering from uræmia save in dire emergency. To the condition of entero-sepsis, intestinal toxæmia, or fæcal or stercoral intoxication, I have already alluded. My own studies and experience with this condition have led me to profound conviction, since time and again I have seen commencing septic wound disturbance aborted by the institution of measures calculated to clear out the alimentary canal, this being true of wounds in all parts of the body. The same is true, also, of the toxæmia produced in puerperal, diphtheritic and scarlatinal cases, in which, as is well known, we operate only when compelled to in the interest of life.

One form of entero-sepsis upon which but little has been written, and yet which furnishes a clue to many fatal cases, especially those connected with abdominal surgery, is that produced by the bacillus coli commune. This, as is well known, is a regular inhabitant of the alimentary canal, and its presence there is presumably connected with the chemistry of digestion. Yet, under certain circumstances, it either escapes or is carried beyond its normal limits, and, entering the portal circulation, perhaps the lymphatics also, appears to set up septic disturbances which are typified by the production of septic peritonitis, and possibly other forms of septicæmia in which the peritoneum does not primarily figure. The subject is an inviting one for further research; the condition has hardly yet been dignified by a proper and distinctive name, though Drs. Welch and Councilman, who should be credited with its discovery, term it "colon infection." It is mentioned here only as one variety of entero-sepsis, and as one in which, perhaps, good results are obtained in such cases as those which the gynecologists often meet with, namely, of incipient septic peritonitis, in which the administration of a large dose of magnesium sulphate appears to provoke not merely catharsis, but absorption of septic fluid from within the peritoneal cavity.

4. *Other acute conditions.* As representatives of this group should be mentioned starvation, scurvy, acute anæmia such as follows the post-febrile and post-puerperal state. By all of these conditions vital resistance is so lowered that infection from within or without is greatly favored.[1]

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[1] Concerning the influence of hunger upon immunity and infection, vide Canalis u. Morpurgo, Fortschritte der Medicin, viii. pp. 693, 729.

5. *Conditions of environment.* Emergency is the only justifiable reason for surgical operation where the hygienic surroundings are bad. Universal experience justifies this statement, but experimental proof of the same is not lacking. The experiments of Trudeau beautifully exemplify this. He inoculated a number of rabbits with tuberculosis, isolated them upon a small island in the Adirondack region, fed them well, gave them every benefit of fresh air and sunlight, and, upon killing them four months later, only one was found to present the slightest evidence of tubercular disease. The same number of rabbits in another group were inoculated in the same way and confined in a dark cellar, amidst damp air with poor ventilation. These became rapidly diseased, and without exception all were notably tubercular. (THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES, vol. xciv., July, 1887, p. 119.)

The popularity of fresh-air missions, the benefit of removal of the poor and ill-fed to good hospitals for operation, and numerous other well-known facts, attest the importance of the matter of environment.

6. *Effect of anæsthetics.* There is good reason to think that chloroform and ether administered for some time may produce such changes in the blood and tissues that vital processes of repair, cell resistance, and chemotaxis may be so far interfered with as to facilitate subsequent infection. In making this statement I feel assured of the corroboration of surgeons generally. Yet I know of no particular researches bearing upon it, and would suggest it as offering a fine field for orginal research.

7. *Effect of antiseptics.* Upon first blush the idea that an antiseptic may favor infection would seem to be essentially opposed to facts. Yet the fact is made clear, both by clinical experience and by experiment. Such an event may happen in more than one way. Mercurial and iodoform poisoning are by no means unknown to the surgeon as arising from the use of these drugs for antiseptic purposes. When this condition is established the case becomes at once one of recent toxæmia, to which I have already alluded. That wounds will fail to unite, and that suppuration will occur in these toxæmic conditions, is well known. The individual is so poisoned that his cell-resistance is diminished or destroyed, and in consequence there is little or no opposition to infection.

The other method is by such chemical reaction between vital fluid and antiseptic agent that decomposition of one or both ensues, the antiseptic itself being decomposed, its properties as such lost, while the tissues upon which it acts may have their constitution so changed as to favor rather than resist infection. The best experimental proof of this statement that I know of has been furnished by Abbott (*Johns Hopkins Hospital Bulletin*, April, 1891). Without rehearsing his experiments with mercuric chloride, let me simply remind you of his conclusions:

1. That under the most favorable conditions a given amount of sublimate has the property of rendering inert only a certain number of

individual organisms, since there is a definite chemical reaction between the bacterial protoplasm and the mercuric salt.

2. That the disinfecting activity of sublimate against organisms is profoundly influenced by the proportion of albuminous material contained in the medium in which the bacteria are present.

3. That the relation between staphylococci and sublimate is not a constant one, since organisms from different sources and of different ages behave differently when exposed to the same amount of the salt for the same length of time.

4. That the organisms which survive exposure may experience a temporary attenuation, which, however, may disappear by successive cultivation. (His other conclusions enumerated are irrelevant here.)

From these studies he justifies the statement which has been frequently made, that to the employment of sublimate solutions upon wound surfaces it is plain that there exist at least two serious objections:

First, that the albumin of the tissues and fluids of the body tends to diminish the strength of, or render entirely inert, the solution employed. Since the surgeon possesses no means by which he can determine the amount of such material with which his solutions are to come in contact, he is therefore never in position to say *à priori* that his efforts at disinfection of a wound are or are not successful.

The second objection is that the integrity of tissues is materially disturbed by the application of solutions of this sort.

There is abundance of evidence to lead to the belief that normal tissues and fluids of the body possess the power of rendering inert many kinds of organisms which may have gained access to them. This function must therefore be diminished or destroyed by agents which bring about alterations in the constitution of these tissues. Such changes are known to follow the application of sublimate solutions, which may cause a condition of superficial necrosis, by which the inroads of infectious organisms are not resisted as they would have been had the tissues been left in their natural condition.

From all of which it would appear best to keep not only those, but all other antiseptic agents away, from absolutely clean flesh surfaces. The experiments of Nuttall, Lubarsch, Von Fodor, Bonome, Springfeld, and others have shown the value of blood serum as an antiseptic, while the experience of all laboratory workers points in the same direction. Such serum will always be poured out, it is presumable, in quantity sufficient to serve not only as a cohesive but as an antiseptic agent.

Just here in passing the query is provoked, What agent can best be used as an antiseptic? We are learning every day that, providing everything else be clean and fresh, wounds such as made by the surgeon will also be clean, and that the dry method of operating is, perhaps, the best of all; but inasmuch as the surgeon is often compelled to disinfect an area which has already become infected, he must perforce employ some actively antiseptic agent. It would appear that for most purposes we find the ideal in peroxide of hydrogen, which not merely destroys living organisms, but by oxidation of all undesirable and infected material acts as a scavenger of the tissues, and, in one phrase, when it can be efficiently employed locally, is the conqueror of sepsis.

While such artificial agents as the peroxide must rank as among the highest of their class, it seems to me that we have yet to learn how to utilize to fullest advantage the properties of blood serum. To be sure, this varies among the different animals, and by the limitations of experimental study we are less familiar with such as are possessed by the serum of the human blood than with those enjoyed by that of various animals. For instance, it is well known that a mouse will die of inoculated anthrax, while a rat will not. Also that if the inoculated mouse receive a few drops of rat blood serum it recovers. Practical advantage has been taken of this principle, and it has been proposed, and even carried out, to inject into consumptive patients blood serum of the goat or dog, which are known to be almost immune from tuberculosis. Bonome has found that staphylococci thrown directly into the blood of young animals are there destroyed much more quickly than in that of old animals, namely, in from ten to twenty-five minutes. (This has a bearing on the effect of old age already alluded to.) This bactericidal action of the blood is enhanced if the poisonous extract of empyemic or rather of any old pus be injected into the animal before the experiment, while the extract of recent or acute pus has no such effect. On the other hand the latter, *i. e.*, the extract from acute pus, appears to diminish the chemotactic or phagocytic power of the cell elements. Water also diminishes this bactericidal power of the blood, and an important inference may be drawn from this with reference to the advisability of infusion of saline or other solutions for the relief of acute traumatic anæmia.

Having discussed immunity and conditions which predispose to infection, let us consider how direct infection may be brought about. Infection may be divided into two varieties: Self- or auto-infection and contact infection, including that from the skin and wound, from the air, and from ingesta. And yet, while making these two varieties, namely, infection from without and from within, it must be stated that infection as such is presumably due to the same organisms in either case, and that such varieties are arbitrary and not founded upon essential differences. The causes which lead to auto-infection have been already alluded to, as well as those cases of contact infection which originate from the air and from improper food. To be sure, the experiments of Kocher, and of others, in the direction of feeding animals with putrid or putrifying material, and then insulting the thyroid or bone-marrow, in the endeavor to provoke acute sepsis by infection from the alimentary canal, have not been sufficient to completely satisfy one that by improper food alone sepsis may be caused. But I would make a sharp distinction between such experiments and their results, and the condition of entero-sepsis, which includes only a condition of toxæmia arising from presumably proper food, undergoing perverted chemical changes within the alimentary canal, and there producing poisons as the result of such changes, which, when absorbed, give rise to deleterious effects.

But contact infection, as it usually occurs, arises from the air or from some other unclean foreign substance which comes in contact with exposed raw surfaces. Air contact, is, on first thought, a most fertile source of trouble. Pasteur and Lister first made us fear the air as the most dangerous medium of all, but we have gradually learned that its dangers in any proper operation locality are so small as scarcely to deserve consideration in comparison with the others to be mentioned. Not that germs may not be deposited from the air just as they are in an improperly protected culture-tube, but that nearly all of these are non-pathogenic, and that they, with the pathogenic forms, are nearly always either washed or wiped away, or are destroyed by the blood serum or the phagocytic action of the cells.

The principal sources of contact infection are to be enumerated as follows:

1. Skin and hair.
2. Instruments.
3. Sponges or their substitutes.
4. Suture materials.
5. The hands of the surgeon and his assistants.
6. Drainage materials.
7. Dressing materials.
8. Miscellaneous, *e. g.*, drops of perspiration, an unclean irrigator-nozzle, the nail-brush, the clothing of the operator or the bystanders, etc.

1. *Skin and hair.* The danger here comes not so much from what may be on the surface as from that which may be contained within the hair-follicles and sebaceous and sudoriparous glands. The prevention of infection from this source, therefore, requires more than ordinary shaving of the surface or superficial application of soap and water. Lister claimed for carbolic solutions that they had the power of impregnating greasy material with their antiseptic virtues, though as the latter are very questionable we must doubt the former. But it is vitally necessary that, by whatever means we may, we should make our pre-

cautions reach into these crypts, for the possibility of the hibernation of infectious organisms in the crypts or even the tissues of the skin has been experimentally proven. This is especially true of the streptococci of erysipelas, which have been found latent, but alive, within the skin long after the subsidence of active manifestations of the disease, the skin having become apparently, at least temporarily, tolerant.

What then are the best means of sterilizing the skin? These must depend upon whether time is afforded for careful preparation or not. When we deliberately do a craniotomy or laparotomy we have ample time for such measures, but when an amputation for injury, time and means are both limited.

In the former instance, there should first of all be a careful shaving of the skin, the razor being, as some Frenchman has described it, an admirable dermal curette. I would prefer, then, to use for a day or two some antiseptic ointment, properly prepared (see No. 8), such as one made with resorcin or lysol, and lanolin, by whose use we may hope to bring about absorption into the skin of the antiseptic employed. After one or two days' use of this, the skin should be again thoroughly washed, and for this purpose the best soap is the sapo viride of the German Pharmacopœia, with 5 per cent. of lysol or hydro-naphthol. Now for an equal period there should be worn over the part a compress kept moist with some liquid, non-irritating antiseptic. For this purpose creolin or lysol, 5 per cent., or hydro-naphthol in saturated cold aqueous solution, perhaps with a little glycerin added, should be worn until the time of operation. Now everything being ready and the patient being anæsthetized, a final scrubbing with hydro-naphthol soap with shaving should be practised, and then the skin washed with equal parts of alcohol and ether or alcohol and turpentine. By this means the operator may feel confident that the surface has been thoroughly disinfected.

In cases of the other class, where time for this programme is not afforded, we must content ourselves with the thorough use of the nail-brush, the razor, and antiseptic soap, with the subsequent use of alcohol and ether upon the skin.

2. *Instruments.* Aside from the information which has long been at hand with regard to the necessity of having clean instruments, I know of nothing so significant as the experience of Thiriar, who had several cases of tetanus following his operations, and whose disastrous experience ceased as soon as he sterilized his instruments by heat. That instruments should be in some way sterilized is now everywhere accepted. The question is now solely with regard to the best method, whether with dry heat, in steam, or by boiling. It appears that the method of dry sterilization injures the instruments, especially those with keen edges, less than any other. For my own part, I prefer a dry sterilizer in which they are subjected for half an hour to a temperature of 140° or 150° C.,

although I prefer to content myself with passing a delicate cutting instrument two or three times through the flame. Long immersion in hot water certainly does injure all edged instruments, as does also superheated steam or hot air.

3. *Sponges.* There appears to be nothing to add in this connection to the well-known directions for cleaning and sterilizing sponges. It is important, however, to know whether a sponge which has once been used can be employed again. A careful series of experiments has convinced me, at all events, that sponges which have been used in non-septic cases, and have been carefully cleansed and immersed in antiseptic solutions for a week or more, contain no bacteria that can reveal themselves after approved culture methods.

Nevertheless, in order to be absolutely on the safe side, it would appear better, in many respects, to use some cheap absorbent material as a substitute for sponges, which can be used once and thrown away. There are numerous materials which we can thus employ, proper care being given only to see that they are both absorbent and sterile. A final cooking or baking shortly before use will insure at least this latter point.

4. *Suture materials.* These are mainly animal or metal; silk, catgut, horsehair, and silkworm-gut being the best examples of the former, and iron, copper, silver wire, of the latter. Two essentials are requisite in all material for suture, namely, strength and sterility. Power of resorption is a secondary consideration, although very necessary in certain cases. We may at once dismiss metal sutures from consideration, since it is the simplest possible measure to sterilize them. But the proper sterilization of animal suture or ligature material is a problem on which a great deal of time has been spent. (See the researches of Brunner and of others.[1])

Silk may be sterilized by boiling, but this weakens it. The best method is to wind it upon glass spools, to drop these into a large test-tube, to plug the tube, and then keep it for an hour in a steam sterilizer, upon two different occasions. Silkworm-gut appears to be much less septic naturally than is catgut, and may be sterilized by immersion in 1 per cent. aqueous sublimate solution for a few hours, and then preservation in alcohol.

But it is with regard to catgut that the greatest study has been excited, and the largest number of preparation methods suggested. It is not necessary here to detain you even with allusion to the work which has been done in this direction, interesting as it may be. Permit me to simply briefly state what I consider the safest and best method by which to insure the sterilization of catgut. The raw gut, preferably that which has been prepared in the factories for surgeons' use, should have, first of all, its fatty material dissolved out by immersion in benzene or ether. It is then allowed to dry and is soaked for one or two days in a 1 per cent. watery solution of corrosive sublimate, after which it is dried and transferred to oil of juniper berries, and from this to strong alcohol containing one per mille of sublimate. (In this, if desired, it can be boiled.) Catgut thus prepared will, so far as we know, resist every attempt to cultivate bacteria from it. If it be desirable to chromicize it, this may be done before it is placed in juniper oil.

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[1] Beiträge zur klinischen Chirurgie, vi. 98; Braatz, Ibid., vii. 70; Klemm, Archiv. f. klin. Chir., xli. 4.

I have, like many others, tried various experiments to accomplish the same results by other means, including moist and dry heat, etc., yet know of nothing which gives such universally satisfactory results as the above.

5. *The hands.* The hands of all those concerned about the field of operation should be carefully disinfected. This includes the surgeon, his assistants, and the nurses or attendants who may handle sponges or dressings. It has not required such laboratory studies as those of Kümmell and others to show that ordinary methods of cleansing the hands do not bring about an aseptic condition. The thousands of times that wound infection has followed contact with the unclean hands of the surgeon or obstetrician bear witness to this fact. It is simply a truism to state that cemeteries have been filled in time past by the septic hands of medical attendants.

How then disinfect them? It would seem almost unnecessary to be obliged to allude here to such measures, yet the use of the penknife and the nail-brush are not always enough. Is it possible for a surgeon to go from the post-mortem room or from a case of erysipelas, or for a surgical teacher to be called from demonstrating on a cadaver to operating in the hospital or in private, without danger of carrying septic material? I think we are now in a position to say Yes, provided he disinfect his own hands and skin, and change his clothing. I know that I have, on numerous occasions, gone directly from a class demonstration on the cadaver to the hospital amphitheatre to operate, and seen patients recover without a sign of sepsis. But how is this possible? Under such circumstances, so far as the hands and forearms are concerned, I would advise to wash them first thoroughly in soap and water, using the nail-brush freely, then to take a tablespoonful or more of flour of mustard and wash the hands thoroughly with this, as if it were a powdered soap. Mustard is certainly an admirable deodorizer, and its essential oil has been shown to be a most valuable antiseptic agent. (This method will serve to disinfect the hands and deodorize them after handling any foul-smelling material or sanious discharge.) Now, before approaching the patient, no matter what may have been done before, aside from the ordinary scrubbing I would highly recommend the use of the sapo viride (G. P.) to which has been added 5 per cent. of lysol, creolin, or hydronaphthol. Hands and forearms should be thoroughly scrubbed with this, then rinsed and immersed in strongly colored solution of permanganate of potassium. They should then be rinsed again, and now immersed in a solution of oxalic acid, not too strong, and yet sufficiently so to decolorize the skin within two or three minutes. The oxalic solution may be rinsed off, and the hands may now be regarded as thoroughly aseptic. It is expected that occasionally during the course of the operation they will be rinsed in antiseptic solution. This, so far as personal experience goes, is a more reliable method than the use of turpentine or any such material upon the hands.

6. *Drainage materials.* For the most part these comprise horsehair, catgut, soft-rubber tubes, hard-rubber tubes, spiral or stiff glass tubes, and gauze strips or wicking. Views and practices concerning drainage have materially changed even since the antiseptic era began. Our predecessors drained to permit escape of pus which they knew would form. Until lately we have drained in order to prevent its formation. We seem now to be on the eve of an era when we need to drain but little or not at all. We resort to drainage now only of necessity, in septic or infected cases. In other cases we drain mainly from habit, or from fear. Indeed, when we start afresh, as it were, without previous infection, the practice of drainage is a confession of fear, or of weakness, both of which are alike unscientific and unfortunate. We have learned that a little blood serum is an advantage rather than a detriment, and we do not need to guard against its presence as we used to. It even seems to me that in many cases, where all other aseptic requirements have been met, we do much more harm than good by the use of drains. Did time permit, it seems to me that it would be justifiable to occupy some moments in a discussion of this single topic. As it is, I will simply justify personal conclusions by mentioning certain classes of operations in which at present I never resort to drainage—never having regretted discontinuing it:

a. Deliberate operations about the brain and calvarium.

b. Amputations when in uninfected tissues.

c. Excisions of joints for conditions other than tubercular.

d. Herniotomy, both for strangulation and radical cure, when the intestine is still viable and no gangrenous condition is met with.

e. Osteotomy, tarsectomy, and other operations for relief of deformity.

f. Most operations for removal of tumors, etc.

This is by no means a complete list, but is simply intended to be suggestive.

7. *Dressing materials.* Two questions come up here: What is the best dressing material? and what antiseptic is most suitable for the case?

Naturally wounds need some protection, and, inasmuch as in certain cases there will be at least a slight discharge of serum or blood, this protection must at the same time be absorbent, and the choice of the absorbent material may well be left to circumstances or to fancy of the surgeon. But the selection of an antiseptic is again a confession of distrust of one's self or of what has been previously done; and while such distrust may be in the interest of the patient, it is not in the direction of scientific advance. Consequently we may say that after the ideal aseptic operation we need only a sterilized and protective dressing—protection from the air without, as well as protection from contact contamination and from the restlessness of the patient. Such ideal dressing may be composed of any sterilized material. The majority of operators, however, desire some additional assurance, or an additional safeguard, which they may, perhaps, secure in the impregnation of the wound-dressing with any one of the more or less reliable antiseptic chemicals. These remarks do not pertain so much to a large group of cases where drainage must be resorted to, and where more or less discharge is necessarily expected. If dressings are to be saturated or much moistened with wound discharges, it is well that they should be charged with some soluble antiseptic. In certain cases the conditions of repair necessitate much purulent or puruloid discharge. It is well that this should be taken up by material which may antagonize its decomposition or putrifaction. Whether this material shall be some soluble salt of mercury or zinc, or something like iodoform, salicylic acid, zinc oxide, etc., is scarcely germane to our present subject; so long as the object aimed at is attained the possibility or probability of wound infection is prevented.

8. *Miscellaneous sources of wound infection.* These are almost too numerous to mention, but illustrative examples of sources of danger may be given as follows:

Drops of perspiration are liable to fall into the wound area from the forehead and face of an excited, fatigued, or hard-worked operator. So also may scales of dandruff from his hair or beard. The former will probably be seen, the latter not. Consequently the ideal operator in this respect is he whose hair is worn short, and whose face is devoid of beard. In almost every clinic are certain irrigator tubes and nozzles intended for daily use. It is quite possible for one of these to be used to day for washing out some old abscess cavity and to be then hung up until to-morrow, when it is used in a case about which pus has neither been present nor is expected to be. Infection may thus be carried from one to the other. It is my custom to disinfect these nozzles with strong solutions of permanganate of potassium, as also the hard-rubber atomizing tubes which I frequently use for spraying out wounds or washing off surfaces.

In many severe cases the surgeon is strongly tempted, sometimes imperatively impelled, to place his hand upon the patient's radial pulse. It has been suggested, and it certainly is good practice, to carefully disinfect the area of the patient's wrist before the operation, so that the operator can, if necessary, feel the pulse without the danger of thereby infecting his hands.

In every well-regulated clinic there are regulations with regard to clothing, and a supply of clean linen is furnished for the operator and his assistants. Some even carry this precaution to the extent of allowing no one in the room who is not thus clad in fresh linen, which will dislodge no dust upon contact. And who shall say that this precaution is not a wise one, even if, perhaps, sometimes superfluous?

Another source of danger, which I have not seen elsewhere alluded to, is one to which of late I have given some personal study. It is customary with many, after the wound is ready for its dressing, to anoint the surrounding skin with some unctuous material, which shall prevent such adhesion of wound-dressing as may make change of the same a source of dread to the patient. In my own clinic this is done almost as a matter of custom. It is quite possible for such ointments to come in contact with the wound; often they are deliberately applied over it. It behooves us, then, to know whether such ointments, which are supposed to be antiseptic, are such in effect. In the surgical clinic of the Buffalo General Hospital ointments containing 5 and 10 per cent. of naphthalin, of resorcin, and of hydro-naphthol are constantly kept on hand. These are made up in part with vaseline, to which lanolin is added. For the purpose of ascertaining in the first place whether the ointment material was or was not sterile, in the second place whether these ointments themselves were reliable, and in the third place whether the method of preparation with or without heat made any difference, a series of experiments has recently been made for me by one of my surgical assistants, Dr. E. J. Meyer, who is also well versed in pharmacy. Briefly, the results of these experiments have been as follows:

1. Vaseline and all other bases commonly supplied for ointments, as they come from the shops, are by no means free from bacterial contamination, the majority of culture experiments made with them being successful.

2. Ointments made with resorcin and naphthalin, even of 10 per cent. strength, prepared without heat, give for the most part growths of various bacteria.

3. Similar ointments made up by the aid of heat, where the temperature of the mass has been raised to the boiling-point of water, seem to be absolutely sterile, and when exposed to the air suffer only from air contamination, so far as found, with non-pathogenic bacteria and the common moulds.

I would regard these experiments as not only suggestive, but important, because they show that there is not enough diffusion of the antiseptic itself through the ointment mass to exert any such effect as has been generally supposed. Therefore, I assign this fact as illustrating another of the possible sources of wound infection from well-intentioned but misjudged and overestimated protection.

It is well to recall here the investigations of Liebreich, who claims that a coating of lanolin constitutes an almost impassable barrier for bacteria, keeping them in or keeping them out, as the case may be.

And now, without detaining you further, it is necessary that I should bring to a close a paper in which the endeavor has been made to be suggestive rather than complete. The particular features to which I would especially invite attention may be epitomized in the following conclusions:

1. Study of wound infection and of the septic condition thereby produced is inseparable from a study of what constitutes immunity.

2. By a study of immunity is furnished the best clue to a due appreciation of the principles of asepsis.

3. The surgery of the future must aim to be aseptic, for, so far as fresh cases are concerned, we have passsed the merely antiseptic era.

4. Asepsis is to be achieved, not alone by attention to the wound and the pharaphernalia of operation, but by the closest regard to the condition of the patient's organs and tissues.

5. Sepsis may arise from circumstances and conditions other than those pertaining to the wound itself, although hitherto practitioners have been too prone to scan solely this field when searching for its cause.

6. Sepsis and infection are combated in more than one way by natural agencies and by inherent properties of cells and fluids, totally aside from the measures which the surgeon institutes, and the wisest man is he who studies to take advantage of these vital activities rather than introduce new and conflicting elements from without.

7. A recognition of the power of chemotaxis possessed by organized and unorganized materials, in such varying degree, can be utilized to great advantage so soon as it can be reasonably clearly defined.

8. A study of chemotactic activity appears to impress one with the truth of the phagocyte doctrine, which, if proven, is one having a large bearing upon the principles as well as the practice of the surgery of the future.

9. The proteid material contained within cellular infectious organisms plays such a rôle, both in causing chemotaxis as well as in poisoning the animal infected, that we have reason to eagerly welcome all knowledge concerning it.

10. So fast as such proteid material can be isolated we need, among other things, to study its effects upon the commonly used antiseptic agents.

11. We need to study much further the anti-toxic and bactericidal properties of human blood serum, and the means by which we can avail ourselves of the same.

12. Some such classification as I have attempted to give of the various causes of lowered resistance to infection, or of the causes of *vulnerability* or susceptibility, will certainly assist in a due appreciation thereof, and will often aid in so fortifying the patient that he may resist infection to which he would otherwise succumb.

13. The condition of entero-sepsis, fecal toxæmia, stercoral intoxication, or whatever it may be called, is certainly one which every practitioner has to fear and against which he should assiduously guard. It is not sufficiently generally recognized and combated.

14. A sub-form of this condition might justly be made and be entitled gastro-sepsis, comprising cases where defective stomach digestion, often from dilatation, brings about a lithæmic or other toxæmic condition which favors infection.

15. Antiseptic agents in the past have worked a revolution in surgical practice and results. We have now reached a time when we know that they all have their disadvantages, and also understand how, if we are strictly aseptic in our work, we can afford to discontinue their application to wound surfaces.

16. But the insurance of the aseptic character of such work necessitates the use of antiseptic agents of some kind upon everything which may directly or indirectly come in contact with these surfaces.

17. When this work is strictly aseptically performed, the use of drains or further employment of antiseptics is either an expression of mental uncertainty or of fear. It may be in the interest of humanity, undoubtedly it often is, but it is not attaining the ideal of scientific work.

TWO CASES OF PREGNANCY WITH BRIGHT'S DISEASE AND ALMOST COMPLETE SUPPRESSION OF URINE.

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AN obstetric physician cannot help being interested in the pathology of puerperal eclampsia. The theory of this disease which has the most reason in its favor is that the convulsions of puerperal eclampsia are caused in the same way as uræmia apart from pregnancy.

But the pathology of ordinary uræmic convulsions appears to me to scarcely yet rest on a firm basis. It seems generally accepted that